

PATENT SPECIFICATION

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(54) OXYGEN-PERMEABLE CONTACT LENS COMPOSITION

(71) We, POLYCON LABORATORIES, INC., a corporation organised under the laws of the State of Arizona, United States of America, of 2131 E. Indian School Road, Phoenix, Arizona, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described, in and by the following statement:—

The present invention relates to an oxygen-permeable composition and to a contact lens fabricated therefrom.

In a further aspect, the invention concerns oxygen-permeable, wetttable transparent copolymers which can be cast, moulded or machined to provide improved contact lenses.

The prior art teaches the use of many different polymeric materials for contact lenses. However, although these polymers possess the optical clarity necessary for corrective lenses, they suffer from other characteristics which reduce their potential utility.

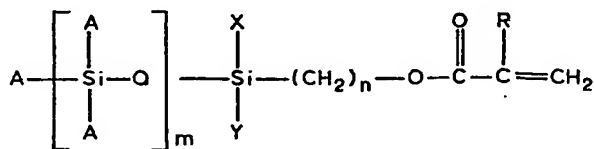
Polymethacrylate is rigid and durable but relatively impermeable to oxygen. The hydrogel materials based on hydrophilic polymers such as polyhydroxyethylmethacrylate are soft and have poor durability. In addition, they provide an environment which is favourable for bacterial growth and are also relatively impermeable to oxygen.

Silicone rubber is soft and resilient and is highly permeable to oxygen. However, due to the low strength of polysiloxanes, a filler which increases the refractive index of the mixture, must be added to improve the durability. Further, the precision machining and polishing which is necessary in the fabrication of a corrective contact lens is extremely difficult with the elastomeric silicone rubbers.

Accordingly, it is highly suitable to provide a polymeric material suitable for use in fabricating contact lenses having increased oxygen permeability, improved mechanical strength, and which is sufficiently rigid to permit precision machining and polishing. The copolymer materials according to the invention possess these properties.

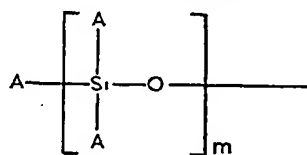
According to the invention, there is provided a copolymer suitable for use in the production of contact lenses having good oxygen permeability comprising:

(a) 10 to 60 parts by weight of at least one polysiloxanylalkyl ester of the structure



wherein

- (1) X and Y are selected from C₁—C₈ alkyl groups, phenyl groups and Z groups,
 (2) Z is a group of the structure

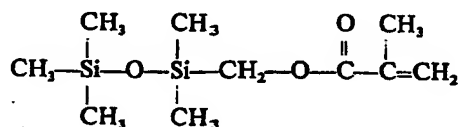


- (3) A is selected from C₁-C₃ alkyl groups and phenyl groups,
 (4) R is a methyl group or hydrogen,
 (5) m is an integer from one to five, and
 (6) n is an integer from one to three,
 (b) copolymerised with 40 to 90 parts by weight of at least one ester of a C₁-C₂₀ monohydric alkanol and acrylic or methacrylic acid.

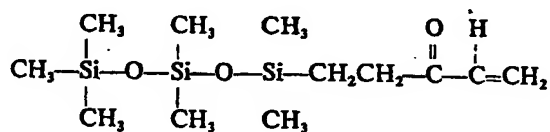
The copolymers according to the invention may be prepared by copolymerising a polysiloxanylalkyl ester of acrylic or methacrylic acid with an alkanol ester of acrylic or methacrylic acid.

Representative polysiloxanylalkyl ester comonomers which may be employed in the practice of the invention include:

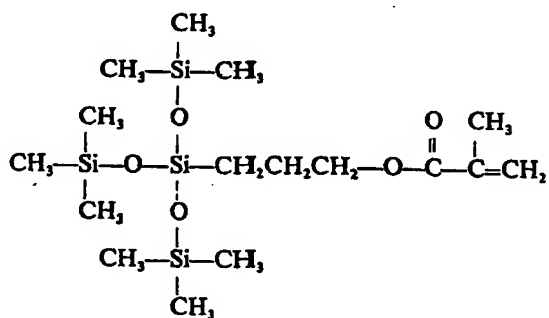
pentamethyldisiloxanymethyl methacrylate



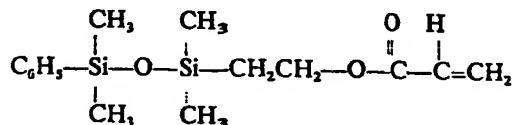
heptamethyltrisiloxanylethyl acrylate,



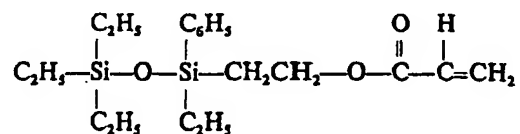
tris(trimethylsiloxy)-p-methacryloxypropylsilane,



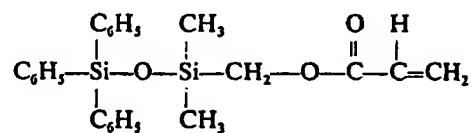
phenyltetramethyldisiloxanylethyl acrylate,



phenyltetraethylidisiloxanylethyl methacrylate,



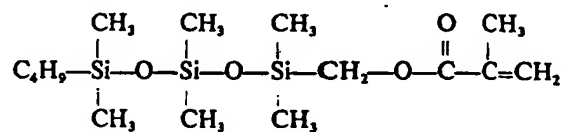
triphenyldimethyldisiloxanylmethyl acrylate,



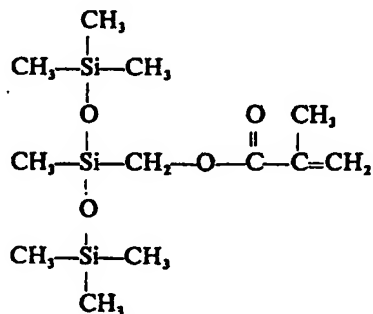
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isobutylhexamethyltrisiloxanylmethyl methacrylate,

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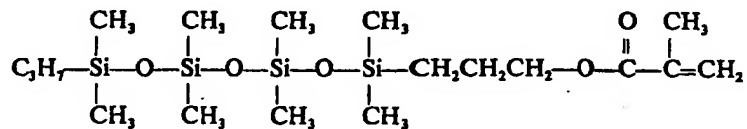


methyldi(trimethylsiloxy)-methacryloxymethylsilane,



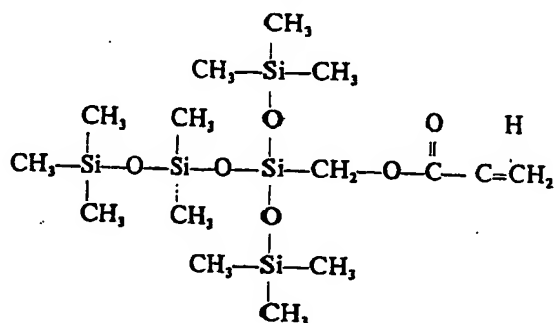
n-propyloctamethyltetrasiloxanylpropyl methacrylate,

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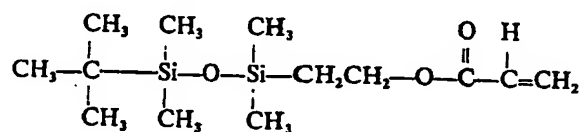


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pentamethyldisiloxydi(trimethylsiloxy)-acryl xymethylsilane,

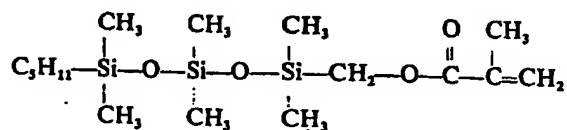


t-butyltetramethyldisiloxanylethyl acrylate,

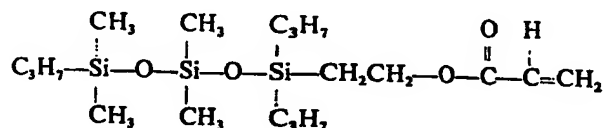


5 n-pentylhexamethyltrisiloxanylmethyl methacrylate,

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tri-i-propyltetramethyltrisiloxanylethyl acrylate,



10 Representative alkanol ester comonomers which may be employed in the practice of the invention include:

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methyl acrylate and methacrylate
 ethyl acrylate and methacrylate
 propyl acrylate and methacrylate
 isopropyl acrylate and methacrylate
 15 butyl acrylate and methacrylate
 amyl acrylate and methacrylate
 hexyl acrylate and methacrylate
 heptyl acrylate and methacrylate
 20 octyl acrylate and methacrylate
 2-ethylhexyl acrylate and methacrylate
 nonyl acrylate and methacrylate
 decyl acrylate and methacrylate
 undecyl acrylate and methacrylate
 25 lauryl acrylate and methacrylate
 cetyl acrylate and methacrylate
 octadecyl acrylate and methacrylate

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At present it is preferred to employ polysiloxanyl acrylate and methacrylate esters which have a straight or branched siloxan chain containing two to four silicon atoms having methyl or phenyl substituents and one to three ethylene groups connecting the siloxanyl chain to the acryloxy or methacryloxy group. Best results are obtained if the polysiloxanyl ester content of the copolymer is up to 35% by weight and correspondingly less, e.g., 10—15%, as the silica contents of the ester is increased. If one employs a branched chain alkanol ester, e.g., 2-ethylhexyl acrylate, one preferably employs a lower polysiloxanyl ester comonomer, e.g., pentamethyldisiloxanylmethyl acrylate.

The copolymers of the invention are prepared by contacting the mixture of comonomers with a free radical generating polymerization initiator of the type commonly used in polymerizing ethylenically unsaturated compounds. Representative free radical polymerization initiators include:

acetyl peroxide
lauroyl peroxide
decanoyl peroxide
caprylyl peroxide
benzoyl peroxide
tertiarybutyl peroxyphthalate
diisopropyl peroxydicarbonate
tertiarybutyl peroctoate
 $\alpha\alpha'$ -azobisisobutyronitrile

Conventional polymerization techniques can be employed to produce the novel copolymers. The comonomer mixture containing between about 0.05—2% by weight of the free radical initiator is heated to a temperature between 30°C—100°C, preferably below 70°C, to initiate and complete the polymerization. The polymerization can be carried out directly on a contact lens of form a lens generally having the desired configuration. Alternatively, the polymerization mixture can be heated in a suitable mold or container to form discs, rods or sheets which can then be machined to the desired shape using conventional equipment and procedures employed for fabricating lenses from polymethyl methacrylate. The temperature is preferably maintained below 70°C in order to minimize the formation of bubbles in the copolymer. Instead of employing the bulk polymerization techniques described above, one can employ solution, emulsion or suspension polymerization to prepare the novel copolymers, using techniques conventionally used in the preparation of polymers from ethylenically unsaturated monomers. The copolymer thus produced may be extruded, pressed or molded into rods, sheets or other convenient shapes which are then machined to produce the contact lenses.

The novel copolymers have vastly increased oxygen permeability in comparison to conventional contact lens materials. For example, a copolymer comprising 35 parts pentamethyldisiloxanylmethyl methacrylate and 65 parts of methyl methacrylate has an oxygen permeability of 500 cc.-mil/100 in.²/24 hr./atm. compared to an oxygen permeability of 34 for polymethyl methacrylate and 13 for polyhydroxyethylmethacrylate. These oxygen permeability values were determined in accordance with ASTM D1434, using a tester which has a 3 "Dow" cell pressure change detection units. Discs were cut to proper size to fit the tester, placed in the apparatus and conditioned a minimum of 16 hours under both vacuum and oxygen. Immediately following the conditioning period, the test was performed by plotting a curve of cell pressure versus time. The slope of the curve was then used to calculate the oxygen transmission rate. In general, the oxygen permeability of the copolymers of the invention is at least 4 times to as much as several hundred times higher than that of lenses prepared from polymethylmethacrylate or the so-called "hydrogel" lenses prepared from polyhydroxyethylmethacrylate.

While some of the novel copolymers are inherently wettable by human tears, it may be necessary to improve the wettability of others. This can be accomplished by several alternate methods. For example, wettability can be imparted to the copolymer by the addition of from about 0.1% to about 10% by weight of one or more hydrophilic monomers to the copolymerization mixture. Such monomers include hydroxyalkyl acrylates and methacrylates wherein the alkyl group contains 1 to 4 carbon atoms, acrylic and methacrylic acid, acrylamide, methacrylamide, N-methylolacrylamid, N-methylolmethacrylamide, glycidyl acrylate and

methacrylate and N-vinylpyrrolidone. Alternatively, the wettability of the surface of contact lenses made from the novel copolymers can be improved by the application of a wetting agent such as, for example, a dilute aqueous solution of alkyl dimethylbenzylammonium chloride, by exposure of the surface to a corona discharge or by chemical treatment of the surface with a strong oxidizing agent such as nitric acid.

The rigidity of the contact lenses prepared from materials useful in the practice of this invention may be varied by changing the ratio of comonomers and/or their chemical composition. Thus, contact lenses prepared from acrylate monomers are more flexible than those prepared from alkyl methacrylate may be copolymer of a polysiloxanylalkyl methacrylate and an alkyl methacrylate may be fabricated into a contact lens which is more rigid than a lens prepared from the copolymer of the corresponding acrylates. The lower the alkyl methacrylate content of the copolymer the more flexible the contact lens prepared therefrom.

The rigidity of a contact lens prepared from the materials useful in the practice of this invention may be increased, if desired, by the incorporation into the copolymer composition of 0.01% to about 2% by weight of a crosslinking monomer such as a polyol dimethacrylate or diacrylate or a polyol acrylic ester of higher functionality, for example, ethylene glycol dimethacrylate, butylene glycol dimethacrylate, neopentyl glycol diacrylate and pentaerythritol triacrylate or tetraacrylate.

The refractive index is an important but non-critical characteristic of a contact lens. Thus, the refractive index of polymethylmethacrylate, the polymer most widely used in the fabrication of contact lenses, is 1.49. The refractive indices of the copolymers useful in the practice of this invention may be varied between 1.35 and 1.50 by varying the ratio and nature of the comonomers. In general, increasing the polysiloxanyl monomer content of the copolymer will decrease its refractive index. The nature of the substituents on the silicon atoms of the polysiloxanyl monomer also importantly affects the refractive index of the copolymer. Lower straight chain alkyl substituents produce copolymers of lower refractive index while polysiloxanyl monomers having phenyl substituents on the silicon atoms yield copolymers having a higher refractive index.

The following examples are presented to illustrate the practice of the invention and not as an indication of the limits of the scope thereof.

EXAMPLE 1.

This example illustrates the synthesis of a representative polysiloxanylalkyl ester comonomer, pentamethyldisiloxanylmethyl methacrylate.

Synthesis of Dimethylchloromethylchlorosilane. Distilled trimethylchlorosilane (635 ml., 5 moles), b.p. 59.9°C., is placed in a 1-liter, 3-necked, round-bottom flask equipped with a magnetic stirrer, a thermometer, a gas inlet tube and a dry-ice cooled reflux condenser whose outlet is connected to a water scrubber. After flushing the apparatus with dry nitrogen for 15 minutes, chlorine gas is introduced through the gas inlet tube and the flask is irradiated by ultraviolet light from a General Electric 15-watt germicidal lamp placed at a distance of 6 in. from the flask. Gaseous hydrogen chloride is evolved and absorbed in the water scrubber which contains a caustic soda solution and a small amount of phenolphthalein. The temperature is maintained in the range 30–40°C. while chlorine is bubbled through the reaction mixture. After 30 hours of photochlorination, 5 moles of hydrogen chloride is evolved, as indicated by the discharge of the pink color in the water scrubber. The product is distilled through a column with 18 theoretical plates and the fraction distilling at 115°C. is collected. The yield of dimethylchloromethylchlorosilane ($d_{25}^{25}=1.07$) is 30%.

Synthesis of Pentamethylchloromethylidisiloxane. 134 ml. dimethylchloromethylchlorosilane (1 mole) and 127 ml. (1 mole) of trimethylchlorosilane are mixed and shaken thoroughly. When 600 ml. of distilled water is added, exothermic hydrolytic reactions occur immediately. The mixture is shaken on a mechanical shaker overnight to complete hydrolysis. The upper oily layer is separated and is dried over anhydrous sodium carbonate. After drying, the product is distilled through a column of 13 theoretical plates and the fraction which distills at 151–152°C. is collected. The yield of pentamethylchloromethylidisiloxane (b.p. 151.8°C., $d_{25}^{25}=0.910$, $n_D^{20}=1.4106$) is 30%.

Synthesis of Pentamethyldisiloxanylmethyl Methacrylate. 30 ml. pentamethylchloromethylidisiloxane (0.14 mole), 13.8 ml. (0.16 mole) distilled methacrylic acid, 21.0 ml. (0.15 mole) triethylamine, 30 ml. xylene and 0.8 g.

hydroquinone are mixed and refluxed for 16 hours. Triethylamine hydrochloride precipitates and is filtered. The filtrate is mixed with 1 g. of hydroquinone and 1 g. of copper powder. Xylene is distilled from the mixture at atmospheric pressure. The distillation apparatus is then connected to a vacuum line and the fraction which distills at 73—75°C. under 4—5 mm. Hg pressure is collected. The yield of pentamethyldisiloxanymethyl methacrylate (b.p. 73—74°C./4 mm. Hg, $d_{20}^{20}=0.910$, $n_D^{20}=1.420$) is 45%.

The disiloxane monomer recovered by distillation contains co-distilled hydroquinone. Purification is accomplished by washing the monomer with aqueous alkali solution containing 25% sodium carbonate and 1% sodium hydroxide until the aqueous layer is colorless. The oily monomer layer is then washed with water until neutral and dried over anhydrous sodium carbonate. The dried monomer is refrigerated until used.

EXAMPLE 2.

This example illustrates the preparation of a representative oxygen-permeable copolymer.

A mixture of 35 parts of the disiloxane monomer of Example 1, 65 parts of methyl methacrylate and 0.004 ml. of tert-butyl peroxyvalate per ml. of monomer mixture is placed in a polypropylene Petri dish to a height of one eighth of an inch. The dish is covered and placed in a vacuum oven which has been purged with nitrogen. The oven is closed and the temperature maintained at 45°C for 20 hours the copolymer disc is hard, colorless transparent and rigid. The oxygen permeability is 500 cc.-mil/100 in.²/24 hr./atm.

A cylindrical plug having dimensions of $\frac{1}{4}$ inch thickness and $\frac{1}{4}$ inch diameter is prepared by copolymerizing the 35/65 disiloxane monomer/methyl methacrylate mixture in a polyethylene cap at 45°C. for 20 hours. The plug is machined, cut, polished and finished to a concavo-convex lens.

EXAMPLES 3—9.

These examples illustrate the preparation and properties of copolymers containing varying proportions of a siloxanyl monomer, methyl methacrylate, and a hydrophilic monomer (hydroxyethyl methacrylate).

Mixtures of the disiloxane monomer of Example 1 (DSM), methyl methacrylate (MMA), hydroxyethyl methacrylate (HEMA) and tert-butyl peroxyvalate (0.004 ml. per ml. of monomer mixture) is polymerized in polyethylene caps under the conditions shown in the following table:

Example	Composition, wt. %			Temp. 2C.	Time hr.	Properties*
	DSM	MMA	HEMA			
3	20	75	5	50	6.5	T, H, R
4	35	60	5	45	20	T, H, R
5	44	50	6	50	48	T, H, SR
6	45	50	5	45	20	T, H, SR
7	45	49	6	70 50	1 16	T, H, SR
8	51	40	9	75	2.5	T, H, SR
9	65	30	5	60	4	NT, S, E

*T=transparent; H=hard; R=Rigid; SR=Semi-rigid;
NT=hazy; S=soft; E=elastomeric

The polymerized plugs are machined and finished in the usual manner to lenses with a concave surface on one side and a convex surface on the opposite side. The lenses are easily wetted by water and an aqueous saline solution.

EXAMPLE 10.

This example illustrates the preparation and properties of a wettable oxygen-permeable terpolymer.

A disc is prepared in the manner described in Example 2 from a mixture of 45 parts of the disiloxane monomer of example 1, 50 parts of methyl methacrylate and 5 parts of hydroxyethylmethacrylate using tert-butyl peroxyvalerate as catalyst. The polymerization is carried out at 45°C. for 20 hours. The resultant disc is colorless, transparent, hard and semi-rigid. The surface of the disc is readily wetted by water and saline solution. The oxygen permeability of the terpolymer is 765 cc.-mil/100 in.²/24 hr./atm.

EXAMPLE 11.

This example illustrates the preparation and properties of a wettable oxygen-permeable terpolymer.

A disc prepared in the same manner described in Example 2 by polymerizing a mixture of 20 parts of the disiloxane monomer of Example 1, 75 parts of methyl methacrylate, 5 parts of hydroxyethyl methacrylate and 0.004 ml. of tert-butyl peroxyvalerate per ml. of monomer mixture, at 50°C. has an oxygen permeability of 135 cc.-mil/100 in.²/24 hr./atm. Lenses cut and matched from the disc are transparent, hard and rigid.

EXAMPLES 12—14.

These examples illustrate the preparation and properties of copolymers of a siloxanyl monomer with various proportions of other methacrylic ester comonomers.

Cylindrical plugs are prepared in the manner described in Example 3 from mixtures of the disiloxane monomer (DSM) of Example 1, methyl methacrylate (MMA), octadecyl methacrylate (ODMA), hydroxyethyl methacrylate (HEMA) and ethylene glycol dimethacrylate (EGDMA) by polymerization at 70°C. for 2.5 hours using tert-butyl peroxyvalerate as catalyst. The properties of lenses prepared from the plugs are shown in the following table:

Example	Composition, wt. %					Properties
	DSM	MMA	ODMA	HEMA	EGDMA	
12	35	30	30	5	0	T, H, E
13	45	30	20	5	0	T, S, E
14	45	38	10	5	2	T, S, R

EXAMPLE 15.

This example illustrates the synthesis of 1,1,1-tris(trimethylsiloxy)methacrylatopropylsilane.

23.8 g. (13.0 ml.) of concentrated sulfuric acid is added slowly with stirring to a mixture of 11.6 g. (14.7 ml.) of absolute ethanol and 16.5 ml. of water. The mixture is cooled in a water bath.

Methacrylatopropyltrimethoxysilane (0.1 mole, 24.8 g.), is mixed with 0.3 mole (39.6 g.) of trimethylacetoxysilane in a flask equipped with a magnetic stirrer. Ethylsulfuric acid (6.5 g.), prepared as described above, is added dropwise from a dropping funnel into the stirred mixture. The flask is cooled during the addition of the ethylsulfuric acid catalyst solution in an ice water bath. After completion of the catalyst addition, the solution is stirred at room temperature for two days. The upper oily layer is then separated, washed with sodium bicarbonate solution, washed with water and then dried over anhydrous sodium sulfate. The product is distilled under vacuum to remove ethyl acetate. The distillation flask is immersed in a water bath whose temperature is maintained at 40—45°C. to prevent premature polymerization of the monomer. The yield of tris(trimethylsiloxy)methacrylatopropylsilane is 86% and the density of the monomer is 0.989 g./cc. at 20°C. The monomer is refrigerated until used.

EXAMPLE 16.

This example illustrates the preparation of a copolymer of methyl

methacrylate with the novel polysiloxanyl ester of Example 15.

A cylindrical plug is prepared by polymerizing a mixture of 40 parts of tris(trimethylsiloxy)- α -methacryloxypropylsilane and 60 parts of methyl methacrylate in the presence of tert-butyl peroxyisobutyrate at 50°C. Lenses prepared from the plug are hard, transparent and oxygen permeable.

EXAMPLE 17—18.

This example illustrates the preparation of various copolymers of polysiloxanyl esters and various alkyl acrylates or methacrylates. The polysiloxanyl ester comonomers are prepared according to the general techniques of Examples 1 and 15. The copolymer is prepared according to the general technique of Example 2. All copolymers resulting are transparent, hard and rigid so as to be suitable for contact lens manufacture. The oxygen permeability of the copolymers varies from 300—500 cc.-mil/100 in.²/24 hr./atm. as measured by the technique previously described.

POLYSILOXANYL ESTER

ALKANOL ESTER

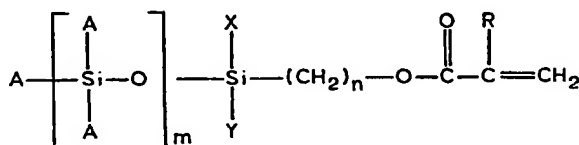
Wt. % in Copolymer	Monomer	Wt. % in Copolymer	Monomer
17	heptamethyltrisiloxanylethyl acrylate	65	2-ethylhexyl acrylate
18	isobutylhexamethyltrisiloxanylmethyl methacrylate	70	t-butyl methacrylate
19	n-propyloctamethyltetrasiloxanylpropyl methacrylate	70	decyl methacrylate
20	tri-i-propyltetramethyltrisiloxanylethyl acrylate	75	isopropyl acrylate
21	t-butyltetramethyldisiloxanylethyl acrylate	75	methyl acrylate
22	n-pentahexamethyltrisiloxanylmethyl methacrylate	80	ethyl methacrylate
23	phenyltetramethyldisiloxanylethyl acrylate	80	octadecyl acrylate
24	phenyltetraethyldisiloxanylmethyl methacrylate	80	hexyl methacrylate
25	triphenyldimethyldisiloxanylmethyl acrylate	85	methyl acrylate
26	tris(trimethylsiloxy)- γ -methacryloxypropylsilane	85	methyl methacrylate
27	methylidyl(trimethylsiloxy)-methacryloxyethylsilane	85	n-propyl methacrylate
28	pentamethyldisiloxydi(trimethylsiloxy)-acryloxyethylsilane	90	ethyl acrylate

As illustrated by Examples 17—28, it is preferred to use a straight chain alkanol ester monomer if the polysiloxanyl ester monomer is a branched chain compound, and vice versa. Also, it is preferred to employ two acrylate or two methacrylate comonomers to prepare the copolymer, rather than an acrylate monomer and a methacrylate monomer. Finally, where more complex polysiloxanyl ester comonomers are employed, the proportion of polysiloxanyl ester is lower, e.g., 10—20%, than if simpler polysiloxanyl esters are employed. In general, the presence of larger, more complex substituents on the interior silicon atoms tend to increase the refractive index of the copolymer, all other factors being equal.

WHAT WE CLAIM IS:—

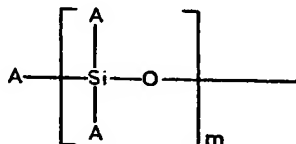
1. A copolymer suitable for use in the production of contact lenses having good oxygen permeability, comprising:

(a) 10 to 60 parts by weight of at least one polysiloxanylalkyl ester of the structure



wherein

- (1) X and Y are selected from $\text{C}_1 - \text{C}_8$ alkyl groups, phenyl groups and Z groups,
- (2) Z is a group of the structure



- (3) A is selected from $\text{C}_1 - \text{C}_8$ alkyl groups and phenyl groups,
- (4) R is methyl group or hydrogen,
- (5) m is an integer from one to five, and
- (6) n is an integer from one to three,
- (b) copolymerised with 40 to 90 parts by weight of at least one ester of a $\text{C}_1 - \text{C}_{20}$ monohydric alkanol and acrylic or methacrylic acid.

2. A contact lens fabricated from the copolymer composition as claimed in claim 1, having a refractive index of from 1.35 to 1.50.

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